Geometric Mean of Test Product (T) and Reference product (R) of Estrone Sulfate - Baseline adjusted (N = 24)

| | Geometric Mean | | | |
|----------------------------------|------------------|-----------------------|--|--|
| Pharmacokinetic Parameter | Test Product (T) | Reference Product (R) | | |
| C _{max} (ng/mL) | 12.1579 | 16.8587 | | |
| AUC ₀₋₂₄ (ng · hr/mL) | 66.5996 | 121.5597 | | |
| t_{max} (hr) | 5.49 | 8.83 | | |

TABLE 40

Statistical Results of Test product (T) versus Reference product (R) for Estrone Sulfate - Baseline adjusted (N = 24)

Geometric Least

| | Square Mean | | | | |
|---|------------------------|-----------------------------|--------------------------|------------------|-------------------------------|
| Pharmacokinetic Parameter | Test Product (T) | Reference Product (R) | Intra Subject CV % | T/R Ratio % | 90% Confidence Interval |
| C _{max} (ng/mL) AUC ₀₋₂₄ (ng · hr/mL) | 12.3350 68.5260 | 16.5470 118.4170 | 48.02 73.87 | 74.55* 57.87* | 59.43-93.51 41.68-80.35 |

^{*}Comparison was detected as statistically significant by ANOVA ($\alpha = 0.05$).

While the pharmaceutical compositions and methods have been described in terms of what are presently considered to be practical and preferred embodiments, it is to be understood that the disclosure need not be limited to the disclosed embodiments. It is intended to cover various modifications and similar arrangements included within the

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spirit and scope of the claims, the scope of which should be accorded the broadest interpretation so as to encompass all such modifications and similar embodiments. This disclosure includes any and all embodiments of the following claims.

The invention claimed is:

- 1. A method for treating moderate to severe dyspareunia in a human subject, the method comprising: inserting about two inches into the vagina of the subject a soft gelatin capsule containing a liquid pharmaceutical composition, wherein the composition comprises about 4 µg to about 25 µg of estradiol and an excipient that increases the viscosity of the composition, wherein the composition has a viscosity from about 50 cP to about 1000 cP at 25° C., and wherein the composition spreads over the vaginal tissue and the estradiol is absorbed by the vaginal tissue.
- 2. The method of claim 1, wherein the subject is in a reclined position while inserting the soft gelatin capsule.
- 3. The method of claim 1, wherein the subject is in a standing position while inserting the soft gelatin capsule.
- **4**. The method of claim **1**, wherein the viscosity of the composition is from about 50 cP to about 380 cP at 25° C.
- 5. The method of claim 1, wherein the excipient that increases the viscosity comprises polyethylene glycol long chain saturated fatty acid esters, ethylene glycol long chain saturated fatty acid esters, or a mixture thereof.
- **6**. The method of claim **1**, wherein the composition comprises 4 μg estradiol or 10 μg estradiol.
- 7. The method of claim 1, wherein the soft gelatin capsule is inserted once daily for two weeks and twice weekly thereafter.

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